

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
12 February 2004 (12.02.2004)

PCT

(10) International Publication Number
WO 2004/013299 A3

- (51) International Patent Classification⁷: **A01K 67/00**, C12N 15/00, G01N 33/00 (74) Agent: ELBING, Karen, L.; Clark & Elbing LLP, 101 Federal Street, Boston, MA 02110 (US).
- (21) International Application Number: PCT/US2003/024322
- (22) International Filing Date: 1 August 2003 (01.08.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/400,900 2 August 2002 (02.08.2002) US
- (63) Related by continuation (CON) or continuation-in-part (CIP) to earlier application:
US 60/400,900 (CON)
Filed on 2 August 2002 (02.08.2002)
- (71) Applicant (for all designated States except US): THE GENERAL HOSPITAL CORPORATION [US/US]; 55 Fruit Street, Boston, MA 02114 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): SEED, Brian [US/US]; 9 Hawthorne Place, 5J, Boston, MA 02114 (US). YANG, Yi [CN/US]; 13 Lilac Court, Cambridge, MA 02141 (US).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:**
— with international search report
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report:
12 August 2004
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: METHODS FOR THE PRODUCTION OF CELLS AND MAMMALS WITH DESIRED GENETIC MODIFICATIONS

(57) Abstract: The present invention features novel methods for generating cell lines and mammals with site-specific genetic modifications of interest. The methods involve homologous recombination between an artificial chromosome having a modification of interest and an endogenous chromosome of a cell. The resulting modified cells can be used in standard methods to generate genetically modified mammals. These mammals can be used in a variety of screening methods to identify compounds useful for the treatment or prevention of disease. Additionally, cells that have been modified to eliminate a mutation associated with a disease can be transplanted into patients for the treatment of a disease.

WO 2004/013299 A3